In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 14-318V

Filed: June 2, 2016

EMILY CULLIGAN,	*	TO BE PUBLISHED
Petitioner,	*	Special Master Hamilton-Fieldman
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Gardasil; Human Papillomavirus (HPV) Vaccine; Statute of Limitations; First Symptom or Manifestation of Onset; Premature Ovarian Failure (POF); Primary Ovarian Insufficiency (POI); Menstrual Cycle; Dismissal
Respondent.	*	

Mark Krueger, Krueger & Hernandez, SC, Baraboo, WI, for Petitioner.
Lara Englund, United States Department of Justice, Washington, DC, for Respondent.

DECISION[1]

This is an action by Emily Culligan ("Petitioner") seeking an award under the National Vaccine Injury Compensation Program (hereinafter "Program").[2] Respondent contends that the petition was untimely filed, and as such should be dismissed. For the reasons set forth below, the undersigned concludes that the petition was untimely filed, and it is therefore hereby dismissed.

I. FACTUAL BACKGROUND

Petitioner was born on June 27, 1984. Pet'r's Ex. 1, ECF No. 7-2. It is unclear when

[1] Because this decision contains a reasoned explanation for the undersigned's action in this case, the undersigned intends to post this decision on the website of the United States Court of Federal Claims, in accordance with the purposes espoused in the E-Government Act of 2002. *See* 44 U.S.C. § 3501 (2012). Each party has 14 days to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b).

[2] The National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 (2012) (hereinafter "Vaccine Act"), provides the statutory provisions governing the Program.

she experienced menarche,[3] but from a reproductive system standpoint, her puberty and adolescence appear to have been uneventful. By the age of 22, she had settled into regular menstrual cycles of every 28 days, with moderate flow for two days followed by two days of light flow. Pet'r's Ex. 6 at 7,[4] ECF No. 7-7.

Petitioner briefly used various forms of hormonal contraception, including the NuvaRing, but did not want to use hormones for any length of time "on general principals [sic]." Pet'r's Ex. 5 at 1, ECF No. 7-6. She had a non-hormonal copper Paragard IUD implanted on November 15, 2006, Pet'r's Ex. 6 at 5-6, ECF No. 7-7, which remained in place until she had it removed in February of 2013, Pet'r's Ex. 2 at 8, ECF No. 7-3. She had a history of cystic acne, for which she was prescribed Spironolactone in early 2011, but no history of hirsutism. *Id.* at 17.

On March 31, 2010, Petitioner saw Laila Sillay, M.D., her gynecologist, for a routine annual examination. *Id.* at 21-23. She reported menstrual cycles that occurred every 25 days and lasted for 5 days. *Id.* at 21. She received her first dose of the HPV vaccine. *Id*. at 22. She received the second dose of the vaccine on June 1, 2010. *Id*. at 20. On October 4, 2010, she was administered the third dose of the HPV vaccine, and she received a seasonal flu vaccine. *Id*. at 19.

Petitioner returned to Dr. Sillay on May 10, 2011, again for a routine examination. *Id.* at 17-18. Her last reported menstrual period was almost three months prior, February 21, 2011, and she reported a six-month history of less frequent, heavier, and longer (7-10 days) menstrual periods. *Id.* at 17. The assessment was oligomenorrhea[5] "likely related to spironolactane, PCOS[6] less likely," and she was given a progestin challenge. *Id.* at 18. The

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[3] Menarche is "the establishment or beginning of menstruation." Menarche, *Dorland's Illustrated Medical Dictionary* (32nd ed. 2012) (hereinafter "*Dorland's*"). Menstruation is "the cyclic, physiologic discharge through the vagina of blood and mucosal tissues from the nonpregnant uterus; it is under hormonal control and normally recurs, usually at approximately four-week intervals, in the absence of pregnancy during the reproductive period (puberty through menopause of the female of the human)." Menstruation, *Dorland's*.

[4] Where, as here, case documents are internally paginated, the undersigned cites to that pagination; where they are not, the undersigned cites to the pagination superimposed by CM/ECF.

[5] Oligomenorrhea is "menstrual flow happening less often than normal, defined as at intervals of 35 days to 6 months, called also *infrequent menstruation*." Oligomenorrhea, *Dorland's*.

[6] Polycystic ovary syndrome, or PCOS, "is a common endocrine system disorder among women of reproductive age" featuring "enlarged ovaries that contain small collections of fluid—called follicles—located in each ovary as seen during an ultrasound exam." Mayo Clinic Staff, Polycystic ovary syndrome: Definition, http://www.mayoclinic.org/diseases-

following week, on May 16, 2011, she returned complaining of pelvic pain. *Id.* at 16. It is not clear whether, at that time, she had started the progestin. *See id.* A pelvic ultrasound was ordered, *id.*, and it showed cysts in both ovaries, *id.* at 14. The impression was "likely ruptured cyst, resolving." *Id.* No bloodwork was done. *See id.*

Petitioner next saw Dr. Sillay on January 15, 2013. *Id.* at 11-13. She reported that her last menstrual period was August 22, 2012, and that she had regular cycles until two years earlier when she developed oligomenorrhea. *Id.* at 11. She had been given Provera in May 2011, which resulted in withdrawal bleeding. *Id.* The assessment was oligomenorrhea, mild acne, and questionable PCOS. *Id.* at 12. She was given another progestin challenge. *Id.*

On February 28, 2013, petitioner saw Dr. Sillay for IUD removal and evaluation of amenorrhea. *Id.* at 8-9. She related a recent history of oligomenorrhea, with cycles every two to three months, and amenorrhea since her wedding in August 2012. *Id.* at 8. She had not responded to the Provera. *See id.* Her IUD was removed, and labs were drawn. *Id.* at 8. A note dated March 4, 2013, indicates that the labs showed elevated FSH and low E2 and progesterone. *Id.* at 7. She was to repeat the labs; if her FSH was still elevated, she would be referred to a reproductive endocrinologist for Primary Ovarian Insufficiency ("POI"). *Id.*

Petitioner returned to Dr. Sillay on March 14, 2013 for the repeat labs. *Id.* at 6. On March 18, 2013, Dr. Sillay made a note that repeat labs had shown "persistently elevated" FSH and low E2, consistent with POI. *Id.* at 5.

On March 24, 2013, Petitioner consulted with Brandon J. Bankowski, M.D., at Oregon Reproductive Medicine. Pet'r's Ex. 8 at 1-4, ECF No. 17-1. He concurred with Dr. Sillay's POI diagnosis.[7] *Id.* at 3. Petitioner and Dr. Bankowski discussed additional testing, including

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conditions/pcos/basics/definition/con-20028841 (last visited May 9, 2016); *see* Pet'r's Ex. 13, Tab 37 at 2, ECF No. 51-3 (Mohd Ashraf Ganie et al., *High prevalence of polycystic ovary syndrome characteristics in girls with euthyroid chronic lymphocytic thyroiditis: a case-control study*, 162 Eur. J. Endocrinology 1117, 1118 (2010)).

[7]Although Dr. Bankowski technically diagnosed Petitioner with Premature Ovarian Failure ("POF")—a term that the parties and the undersigned initially used to define Petitioner's injury— it became clear from the literature filed by the experts that POI "is the preferred term for the condition that was previously referred to as [POF]. . . . The condition is considered to be present when a woman who is less than 40 years old has had amenorrhea for 4 months or more, with two serum FSH levels (obtained at least 1 month apart) in the menopausal range." *See* Pet'r's Ex. 15, Tab 1 at 1, ECF No. 53-2 (Lawrence Nelson, *Primary Ovarian Insufficiency*, 360 New Eng. J. Med. 606, 606 (2009)) (hereinafter "Nelson" with pincites to Petitioner's pagination); *see also* Resp't's Ex. A.29, ECF No. 67-1 (also providing Nelson). Therefore, the undersigned will refer to the condition as POI.

genetic testing, as well as testing for antiovarian, thyroid, and adrenal antibodies. *Id.* They also discussed pregnancy alternatives, including egg donation and gonadotropin IUI. *Id.* Genetic testing showed a normal female karyotype (46, xx), and was negative for fragile X syndrome. *Id.* at 5-10. An ovarian antibody screen was also negative. Pet'r's Ex. 3 at 8, ECF No. 7-4.

Petitioner underwent a pelvic ultrasound on April 19, 2013, which showed a cyst on her right ovary, and a trilaminal endometrium. *Id.* at 5. A repeat pelvic ultrasound on May 15, 2013, showed a homogenous endometrium. *Id*. at 3. A third pelvic ultrasound performed on June 6, 2013, showed a likely intraovarian cyst in the right ovary, but was otherwise normal. Pet'r's Ex. 4 at 2, ECF No. 7-5.

II. PROCEDURAL BACKGROUND

On April 18, 2014, Petitioner filed the present action alleging that the Human Papillomavirus vaccinations ("Gardasil" or "HPV" vaccines) administered to her on March 31, 2010, June 1, 2010, and October 4, 2010 caused her to suffer from POI. Pet., ECF No. 1. Petitioner was, and continues to be, represented by Mark Krueger of Krueger & Hernandez, S.C. Pet. at 2. The case was initially assigned to Special Master Christian Moran. Notice of Assignment, ECF No. 2.

Petitioner filed eight medical record exhibits between May 20 and July 21, 2014, *see* Docket Report; in the interim, the case, along with several others filed by petitioners who had alleged similar injuries caused by Gardasil, was reassigned to the undersigned. *See* Order Reassigning Case, ECF No. 14. Petitioner filed a statement of completion on July 30, 2014. Statement of Completion, ECF No. 19.

On August 14, 2014, Respondent filed a Rule 4(c) Report and Motion to Dismiss ("Respondent's Report"), in which she contended that Petitioner was not entitled to a Program award. Resp't's Report at 3-5, ECF No. 20. Respondent argued that the first symptom of Petitioner's POI was oligomenorrhea, which Petitioner experienced in "late 2010"; accordingly, Petitioner's claim was untimely under the Vaccine Act's statute of limitations. *Id.* at 4 (citing 42 U.S.C. § 300aa-16(a)(2) (2012) (requiring that vaccine-related injury petitions be filed prior to "expiration of 36 months after the date of the occurrence of the first symptom or manifestation of onset . . . of such injury")). Respondent also argued that, even if Petitioner's claim was not time-barred, Petitioner had failed to prove causation under *Althen v. Sec'y of HHS*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). *Id.* at 4-5.

At a status conference held on September 23, 2014, the undersigned discussed with the parties the necessity of establishing when the statute of limitations began to run in the instant

case–and in the other cases in which Mr. Krueger had alleged that petitioners' POI had been caused by Gardasil vaccinations–in order to assess timeliness. *See* Scheduling Order (Sept. 25, 2014), ECF No. 22. The undersigned directed Petitioner to begin the process of identifying all of the POI petitioners so that an assessment of timeliness could take place in all of those cases. *Id*.

On October 1, 2014, Petitioner filed a status report in which she identified eight POI cases[8] to be included in the undersigned's assessment of timeliness. *See* Pet'r's Status Report (Oct. 1, 2014). Petitioner subsequently named the instant case as the "test case" for timeliness. *See* Pet'r's Status Report (Nov. 5, 2014) at 1, ECF No. 25.

A third status conference was held on November 20, 2014, during which the parties agreed that "in all pending [POI] cases . . . an expert hearing [would] be held to address the question of what constitutes 'the first symptom or manifestation of [POI] onset recognized as such by the medical profession at large.'" Scheduling Order (Nov. 24, 2014) at 1, ECF No. 26 (citing *Cloer v. Sec'y of HHS*, 654 F.3d 1322, 1340 (Fed. Cir. 2011) (en banc)). The undersigned explained that a timeliness determination would be made on the basis of the evidence presented at the *Culligan* hearing; similar hearings would *not* be conducted in the other POI cases, all of which would trail *Culligan* for purposes of timeliness determinations. *Id*. The undersigned also added four additional POI cases[9] to the list of cases set to trail *Culligan*. *Id*. The undersigned also ordered that all parties seeking to be joined in the omnibus proceeding consent to share their medical records, *see* Scheduling Order (Nov. 24, 2014) at 2, *Culligan*, ECF No. 26, and all parties later obliged.

The parties and the undersigned proceeded to identify questions for the experts (to be researched and answered before the hearing) regarding the nature and timing of the first symptom or manifestation of onset of POI in the aforementioned cases. *See, e.g.*, Order (Feb. 18, 2015) at 1, ECF No. 37; Scheduling Order (Jan. 30, 2015) at 1, ECF No. 36; Pet'r's Status Report (Dec. 29, 2014) at 1, ECF No. 31; Scheduling Order (Nov. 24, 2014) at 2; Resp't's Status Report (Oct. 28, 2014) at 1, ECF No. 24. The parties and their experts ultimately agreed that, except in *Culligan*, in which the entire medical record would be considered by the experts, the experts would "offer opinions regarding the onset issues in the trailing cases by considering the facts of those cases as hypotheticals." Joint Status Report (Jan. 20, 2015) at 1, ECF No. 33. To

[8] Other than the instant case, Petitioner identified *Alexander v. Sec'y of HHS*, 14-868V; *Tilley v. Sec'y of HHS*, 14-818V; *Fishkis v. Sec'y of HHS*, 14-527V; *Lee v. Sec'y of HHS*, 14-258V; *Lydia McSherry v. Sec'y of HHS*, 14-154V; *Meghan McSherry v. Sec'y of HHS*, 14-153V; and *Laughlin v. Sec'y of HHS*, 13-289V. Pet'r's Status Report (Oct. 1, 2014) at 1, ECF No. 23.

[9] The four added cases were *Chenowith v. Sec'y of HHS*, 14-996V; *Bello v. Sec'y of HHS*, 13-349V; *Olivia Meylor v. Sec'y of HHS*, 10-771V; *Madelyne Meylor v. Sec'y of HHS*, 10-770V. *Id.* The petitioners in these cases are all represented by Mr. Krueger.

facilitate this process, Petitioner filed summaries of the facts of all twelve POI cases. *See* Pet'r's Ex. 9, ECF No. 34-2.[10] Except in *Culligan*, the experts were to rely on the factual summaries, in lieu of the medical records themselves, to articulate their opinions regarding timeliness. *See* Joint Status Report (Jan. 20, 2015) at 1.

At a status conference held on January 28, 2015, the undersigned set deadlines for the parties' expert reports regarding timeliness. *See* Order (Jan. 30, 2015) at 2. The experts were directed to address all of the identified timeliness questions separately, "on a question-by-question basis." *Id*. at 1.

On February 19 and March 3, 2015, three additional cases,[11] all filed by Mr. Krueger, were added to the list of POI trailing cases. *See* Scheduling Order (Mar. 3, 2015) at 1, ECF No. 45; Scheduling Order (Feb. 19, 2015) at 1, ECF No. 38. Mr. Krueger subsequently filed factual summaries of the three new cases. *See* Pet'r's Exs. 10, 11, 12, ECF Nos. 40-2, 41-2, 44-2.

On March 12, March 13, and April 29, 2015, Petitioner filed expert reports and supporting medical literature, all of which were purportedly limited to the issue of timeliness. *See* Pet'r's Ex. 13, ECF Nos. 47-2 to 51-6; Pet'r's Ex. 15, ECF Nos. 53-1 to 54-3; Pet'r's Ex. 17.[12] The expert reports were authored by Dr. Felice Gersh and Dr. Orit Pinhas-Hamiel. *See* Pet'r's Ex. 13, Tab 1; Pet'r's Ex. 15, Tab 1. The reports filed by Dr. Gersh and Dr. Hamiel reflected that they had reviewed the medical records underlying all of the POI cases. *See* Pet'r's Ex. 13, Tab 1 at 12-13; Pet'r's Ex. 15, Tab 1 at 17.

The undersigned convened a status conference on April 1, 2015, after having reviewed Petitioner's expert reports. *See* Scheduling Order (Apr. 2, 2015) at 1, ECF No. 55. The undersigned noted that, "notwithstanding the fact that Petitioner's onset experts have now reviewed the medical records associated with every [POI] case, Respondent's onset expert(s) will review only the cases' factual summaries, the *Culligan* record, and Respondent's list of hypothetical questions." *Id*. Also, having expressed some concern about the extent to which

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[10] A factual summary for another trailing POF case–*Smith*, 14-1107V–was also filed in *Culligan*. *See* Order Appendix (Feb. 23, 2015) at 2-3, ECF No. 39-1; *see also* Order (Jan. 30, 2015) at 1-2, ECF No. 36; Order (Jan. 26, 2015), ECF No. 35. The petitioner in *Smith* was represented by different counsel.

[11] The cases were *Brayboy v. Sec'y of HHS*, 15-183V; *Garner v. Sec'y of HHS*, 15-143V; and *Vakalis v. Sec'y of HHS*, 15-134V.

[12] Petitioner filed Exhibit 17 via compact disc. *See* Notice of Intent to File on Compact Disc (Apr. 29, 2015), ECF No. 56.

Petitioner's expert reports reflected an understanding of the relevant question regarding timeliness, the undersigned reiterated the following:

> [T]he relevant date, for purposes of assessing onset under *Cloer*, is *not* the first point in time at which a definitive diagnosis could have been made; rather, it is the time at which the first symptom or manifestation of the allegedly vaccine-caused injury occurred. The onset experts must make this assessment with the benefit of hindsight, rather than placing themselves in the shoes of the treating, diagnosing physicians. The parties are directed to address this issue as specifically as possible in their pre-hearing briefs.

Id. (full citation omitted).

Respondent then filed an expert report regarding timeliness, as well as relevant medical literature, on May 8, May 28, and June 1, 2015. Resp't's Ex. A to A.32, ECF Nos. 57-1 to 59-6, 63-1 to 63-3, 66-1 to 67-4. Respondent's expert report was authored by Dr. David Frankfurter. Resp't's Ex. A at 6.

At a status conference held on May 14, 2015, Respondent confirmed that, in preparing his expert report, Dr. Frankfurter had reviewed only the factual summaries submitted by Petitioner (and the medical record from *Culligan*). *See* Order (May 15, 2015) at 1, ECF No. 61. Mr. Krueger agreed that, notwithstanding the fact that his experts had reviewed all of the medical records in all of the POI cases, "his experts would be referring to the factual summaries rather than to the medical records themselves" at the timeliness hearing. *Id.*

The parties filed their pre-hearing briefs simultaneously on June 1, 2015, *see* Pet'r's Prehearing Submissions, ECF No. 65; Resp't's Prehearing Submissions, ECF No. 69; and the hearing took place on June 16 and 17, 2015, *see* Minute Entry (June 18, 2015). Petitioner's experts, Dr. Gersh and Dr. Hamiel, and Respondent's expert, Dr. Frankfurter, testified. Tr. at 4, 255, ECF Nos. 81, 83.

On July 1, 2015, the undersigned issued an order identifying nine POI cases[13] "as presumptively precluded under the applicable statute of limitations." Order (July 1, 2015) at 1, ECF No. 79. *Culligan* was included among the presumptively precluded cases. *Id.* The

[13] *Culligan*, *Chenowith*, *Fishkis*, *Garner*, *Lee*, *Lydia McSherry*, *Meghan McSherry*, *Madelyne Meylor*, and *Stone*. Order (July 1, 2015) at 1.

undersigned also identified six cases[14] that appeared to have been timely filed. *Id*. Having apprised the parties of these preliminary conclusions, the undersigned granted them additional time to file status reports identifying the cases in which they intended to contest this determination, and explaining what they had identified as the first symptom or manifestation of onset in each of those cases. *Id*. at 2.

On August 28, 2015, Respondent filed a status report in which she stated that she did not intend to contest the undersigned's preliminary findings in any of the presumptively timely cases filed by Mr. Krueger. Resp't's Status Report (Aug. 28, 2015) at 1, ECF No. 84. In status reports filed on September 2 and 30, 2015, Petitioner argued that all of the preliminarily precluded cases were, in fact, timely. *See* Pet'r's Status Report (Sept. 2, 2015) at 2-7, ECF No. 85 (addressing *Culligan*, *Chenowith*, *Garner*, *Lee*, *Lydia McSherry*, and *Madelyne Meylor*); Pet'r's Status Report (Sept. 30, 2015) at 1-2, ECF No. 87 (addressing *Fishkis*, *Meghan McSherry*, *Stone*).

At a status conference held on October 13, 2015, the undersigned "informed the parties that, for purposes of an onset determination, the [POI] cases [would] be divided [into] two groups: petitioners who never menstruated . . . and the rest of the [POI] petitioners." *See* Scheduling Order (Oct. 14, 2015) at 1, ECF No. 88.

Relevant post-hearing briefing[15] concluded on January 20, 2016. *See* Pet'r's Post Hr'g Br., ECF No. 91; Resp't's Post Hr'g Br., ECF No. 94; Pet'r's Post Hr'g Reply Br., ECF No. 95. Petitioner's claim is now ready for a determination of the first symptom or manifestation of onset of the alleged vaccine-related injury; and, relatedly, whether the Vaccine Act's statute of limitations bars the claim.

III. ANALYSIS

A. Applicable Legal Standard

Section 300aa-16(a)(2) of the Vaccine Act provides that, regarding

> a vaccine set forth in the Vaccine Injury Table which is administered after [October 1, 1998], if a vaccine-related injury occurred as a result of the administration of such vaccine, no petition may be filed for compensation under

[14] *Alexander*; *Bello*, *Brayboy*, *Olivia Meylor*, and *Vakalis*. *Id.* The undersigned also identified as timely *Smith*, a trailing POF case that had been filed by a different attorney. *Id.* In *Tilley*, the undersigned directed the parties to file additional briefs regarding timeliness. *Id.*

[15] Briefing addressing Petitioner's request for interim attorneys' fees is not relevant to the timeliness issue and is therefore not included in this discussion.

> the Program for such injury after the expiration of 36 months after the date of the occurrence of the first symptom or manifestation of onset . . . of such injury.

42 U.S.C. § 300aa-16(a)(2).

This statute of limitations is not triggered by the administration of the vaccine, but "begins to run on the date of occurrence of the first symptom or manifestation of onset of the vaccine-related injury for which compensation is sought." *Cloer*, 654 F.3d at 1335. "[E]ither a 'symptom' or a 'manifestation of onset' can trigger the running of the statute [of limitations], whichever is first." *Markovich v. Sec'y of HHS*, 477 F.3d 1353, 1357 (Fed. Cir. 2007).

"[I]t is the first symptom or manifestation of an alleged vaccine injury, not first date when diagnosis would be possible, that triggers the statute of limitations." *Carson ex rel. Carson v. Sec'y of HHS*, 727 F.3d 1365, 1369 (Fed. Cir. 2013), *reh'g & reh'g en banc denied*, 2013 WL 4528833 at *1. "A symptom may be indicative of a variety of conditions or ailments, and it may be difficult for lay persons to appreciate the medical significance of a symptom with regard to a particular injury." *Markovich*, 477 F.3d at 1357. While the symptom of an injury must be recognized as such "by the medical profession at large," *Cloer*, 654 F.3d at 1335, even subtle symptoms that a petitioner would recognize "'only with the benefit of hindsight, after a doctor makes a definitive diagnosis of injury,'" trigger the running of the statute of limitations, whether or not the petitioner or even multiple medical providers understood their significance *at the time*. *Carson*, 727 F.3d at 1369-70 (quoting *Markovich*, 477 F.3d at 1358).[16]

There is no explicit or implied discovery rule under the Vaccine Act. *Cloer*, 654 F.3d at 1337. The date of the occurrence of the first symptom or manifestation of onset of the alleged vaccine-related injury "does not depend on when a petitioner knew or reasonably should have known anything adverse about her condition." *Id.* at 1339. Nor does it depend on when a petitioner knew or should have known of a potential connection between an injury and a vaccine. *Id.* at 1338 ("Congress made the deliberate choice to trigger the Vaccine Act statute of limitations from the date of occurrence of the first symptom or manifestation of the injury for which relief is sought, an event that does not depend on the knowledge of a

[16] Petitioner argues that "POI is a latent injury" and that "the first symptom of onset, in terms of the applications [sic] of the statute of limitations, can be subtle and can precede manifestation of onset by months or even years." Pet'r's Post Hr'g. Br. at 9. This argument has been made before: the Court of Federal Claims, in *Setnes v. United States*, 57 Fed. Cl. 175 (2003), "was concerned with the very subtle symptoms attributed with autism that can be easily confused with typical child behavior, and it distinguished the terms 'symptom' and 'manifestation.'" *Markovitch*, 477 F.3d at 1357-58. The *Setnes* court's interpretation of the "first symptom or manifestation of onset" language of the statute was rejected by *Markovich*, a ruling that has since been reaffirmed by the Federal Circuit en banc in *Cloer*. 654 F.3d at 1334-1335.

petitioner as to the cause of an injury."); *see Markovich*, 477 F.3d at 1358 ("Congress intended the limitation period to commence to run prior to the time a petitioner has actual knowledge that the vaccine recipient suffered from an injury that could result in a viable cause of action under the Vaccine Act." (internal quotation marks omitted)).

B. Symptoms of POI Onset, Including Criteria for Distinguishing "Symptom" from "Normal"

Primary ovarian insufficiency can begin abruptly, *see* Tr. at 69; *see also* Nelson at 2-3; but it may also develop over several years, *see* Tr. at 70, 198-99, 398; *see also* Nelson at 2-3; Pet'r's Ex. 17, Tab 50 at 2 (Paolo Beck-Peccaz & Luca Persam, *Premature Ovarian Failure*, 1 Orphanet J. Rare Diseases, at 2 (Apr. 2006) (hereinafter "Beck-Peccaz")). Thus, a woman could have symptoms of POI for several years before actually ceasing menstruation or being diagnosed with POI. *See* Tr. at 70, 198-99, 398*; see also* Tr. at 319; Nelson at 2-3; Beck-Peccaz at 2. The experts agreed that the symptoms of POI include menstrual irregularities, including primary and secondary amenorrhea,[17] cycle and frequency irregularity, and excessive or prolonged bleeding; delayed menarche; lack of breast development and poor growth velocity; night sweats; hot flashes; sleep disturbances; mood changes; recurring ovarian cysts; arrested puberty; and marked hirsutism. Tr. at 38, 57, 68-69, 116-17, 319, 366. Most of these symptoms are not "normal" for a woman under the age of 40. Petitioner therefore does not dispute that they can constitute the "first symptom or manifestation of onset" of POI for purposes of the Act's statute of limitations, and there was little discussion of the symptoms beyond their inclusion on the list of symptoms. As to menstrual irregularities and delayed menarche, however, Petitioner and Petitioner's experts dispute that these two conditions should be considered symptoms at all, because many young women experience these conditions at the beginning of their reproductive lives, such that these conditions are considered "normal." *See, e.g.*, Pet'r's Post Hr'g Br. at 2, 4-8; Tr. at 32, 58, 61, 72-73, 170-71; *see also* Tr. at 380 (Respondent's expert, Dr. Frankfurter, explaining that it is normal for a teenager to have irregularity, albeit within a range). As a result, Petitioner and her experts claim, menstrual irregularity only constitutes a symptom or manifestation of onset of POI when that irregularity is effectively considered secondary amenorrhea. Pet'r's Post Hr'g Br. at 4-5; Pet'r's Post Hr'g Rep. Br. at 3.

By instead finding that "normal" menstrual irregularity is a symptom for purposes of the Act's statute of limitations, Petitioner argues, the undersigned will somehow increase Petitioner's burden of proof. *See* Pet'r's Post Hr'g Reply Br. at 1-2. The undersigned does not

[17] Amenorrhea is "absence or abnormal stoppage of the menses." Amenorrhea, *Dorland's*. Primary amenorrhea is "failure of menstruation to occur at puberty." Primary Amenorrhea, *Dorland's*. Secondary amenorrhea is "cessation of menstruation after it has once been established at puberty." Secondary Amenorrhea, *Dorland's*.

agree. The undersigned does agree, however, that to qualify as the first symptom or manifestation of onset under the Act, a condition must be a symptom of something amiss, however subtle; it cannot be "normal": a symptom is "[a]ny morbid phenomenon *or departure from the normal* in structure, function, or sensation, experienced by the patient and indicative of disease." Symptom, *Stedman's Medical Dictionary* (28th Ed. 2013) (hereinafter "*Stedman's*") (emphasis added); *accord Markovich*, 477 F.3d at 1360 (observing that eye blinking episodes constituting first symptom of child's seizure disorder "were not normal child behavior"). In order to determine the date of the first symptom or manifestation of onset of the vaccine-related injury, therefore, a method for separating "normal" menstrual irregularities from abnormal symptoms of POI is necessary.[18]

Fortunately, medical literature provided by the parties provides a solution, both simple and elegant. *See* Resp't's Ex. A.2, ECF No. 57-4 (Comm. on Adolescent Health Care, Am. Coll. of Obstetricians & Gynecologists, *Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign*, Comm. Op. No. 349 (Nov. 2006)) (hereinafter "ACOG Opinion" or "ACOG Op."); *see also* Pet'r's Ex. 15, Tab 4. In *Cloer* and *Markovich*, the Federal Circuit directed that "the symptom or manifestation of onset must be recognized as such by the medical profession at large." *Cloer*, 654 F.3d at 1335; *Markovich*, 477 F.3d at 1360. The ACOG Opinion is an opinion from the Committee on Adolescent Healthcare at the American College of Obstetricians and Gynecologists, together with the American Academy of Pediatrics, entitled "Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign." *See* ACOG Op. It was issued in November 2006, and "Reaffirmed" in 2009. ACOG Op. at 1. The abstract of the ACOG Opinion provides:

> It is . . . important for clinicians to have an understanding of bleeding patterns in girls and adolescents, the ability to differentiate between normal and abnormal menstruation, and the skill to know how to evaluate young patients' conditions appropriately. Using the menstrual cycle as an additional vital sign adds a

[18] Petitioner also argues that irregular menstruation should not be considered the first symptom of POI because it "can be explained by other causes." Pet'r's Post Hr'g Reply Br. at 2-3. This argument has been repeatedly rejected by the Federal Circuit, and is equally as unpersuasive here. A symptom need not be exclusive to the particular injury alleged in order to be "the first symptom" of that injury for purposes of the Act. *See Markovich*, 477 F.3d at 1357 ("A symptom may be indicative of a variety of conditions or ailments, and it may be difficult for lay persons to appreciate the significance of a symptom with regard to a particular injury."); *see also Carson*, 727 F.3d at 1370 (holding that even where "[t]here is no question that speech delay can be indicative of several conditions, and in some circumstances may even be normal . . . it was not arbitrary and capricious for the Chief Special Master to find that the severe speech delay . . . was the first objectively recognizable symptom of autism, the alleged vaccine injury.")

> powerful tool to the assessment of normal development and the exclusion of serious pathologic conditions.

Id. The article goes on to discuss a number of articles and robust epidemiological studies concerning what constitutes "normal menstrual cycles in young females," including age at menarche, and "cycle length and ovulation," *id.* at 2-3; "abnormal menstrual cycles," including "prolonged interval[s]," *id.* at 3-4; and "excessive menstrual flow," *id.* at 4. The article concludes with a chart, reproduced below, that together with one difference applicable to women older than 18, provides comprehensive guidance to the "medical profession at large" about when menstrual irregularities have exceeded "normal" variation to become symptoms of a potential problem. *Id.* at 4-5. The chart is as follows:

Menstrual Conditions That May Require Evaluation

Menstrual periods that:

- Have not started within 3 years of thelarche[19]
- Have not started by 13 years of age with no signs of pubertal development[20]
- Have not started by 14 years of age with signs of hirsutism[21]
- Have not started by 14 years of age with a history or examination suggestive of excessive exercise or eating disorder
- Have not started by 14 years of age with concerns about genital outflow tract obstruction or anomaly
- Have not started by 15 years of age[22]

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[19] Thelarche is "the beginning of development of breasts in the female." Thelarche, *Stedman's*.

[20] Pubertal development is measured by assessing an individual's stages of puberty using the Tanner growth chart, which is "based on pubic hair growth, development of genitalia in boys, and breast development in girls." Tanner stage, *Stedman's*. For purposes of the ACOG criteria, the undersigned considers Tanner stages I (child) and II (prepubertal) as showing "no signs of pubertal development," and Tanner stages III (early pubescent) and IV (late pubescent) as showing such signs. Dr. Frankfurter testified that a young woman who has never menstruated and who has no signs of secondary sexual development by age 13 should be evaluated. Tr. at 377.

[21] Hirsutism is the "presence of excessive bodily and facial hair, usually in a male pattern, especially in women." Hirsutism, *Stedman's*.

[22] At the hearing, Doctors Hamiel and Gersh opined that an adolescent who has not reached menarche by age 16 should be evaluated for primary amenorrhea. Tr. at 92, 238. Dr. Frankfurter opined that the age of evaluation should be 15 years. Tr. at 365. Both the ACOG Opinion and Dr. Hillard, author of medical literature introduced by Petitioner, acknowledge that the traditional definition of primary amenorrhea has been no menarche by age 16. ACOG Op. at

- Are regular, occurring monthly, and then become markedly irregular[23]
- Occur more frequently than every 21 days or less frequently than every 45 days[24]
- Occur 90 days apart even for one cycle[25]
- Last more than 7 days
- Require frequent pad or tampon changes (soaking more than one every 1-2 hours)

Id. at 5.

Hillard reproduces this chart, accompanied with this caution:

> Failure to evaluate teens who meet the criteria cited in the [ACOG] Opinion can be a significant disservice to young women, leading to unnecessary discomfort, embarrassment, poorer quality of life, adverse self esteem, and current or future health risks such as anemia and low bone mineral density, as well as potential metabolic and cardiovascular risks. . . . [J]ust as with other vital signs like pulse and respiration, *[menstrual cycle] values outside of statistically derived normal parameters may signal disease or derangements in normal health.*

Hillard at 8 (emphasis added). The ACOG criteria and chart were also translated into lay person's terms and posted for public access on the Womenshealth.gov website. *See* Pet'r's Ex. 20.

2; Pet'r's Ex. 15, Tab 4, at 5, ECF No. 53-5 (Hillard, Paula, *Menstruation in Adolescents: What Do We Know? and What Do We Do with the Information?*, 27 J. Pediatric Adolescent Gynecology 309 (2014)) (hereinafter "Hillard" with pincites to Petitioner's pagination). However, both articles note that 95-98% of females will have experienced menarche by age 15, and that delays in evaluating these young women can result in delays in detection and treatment of significant disorders, including POI. ACOG Op. at 2; Hillard at 6.

[23] At the hearing, Dr. Hamiel testified that she would recommend further evaluation of a non-adolescent woman whose cycle had been regular (21-35 days) and then became irregular (less frequent than every 35 days). Tr. at 67.

[24] For women over the age of 18, this criterion is more frequently than every 21 days or less frequently than every 35 days. *See* ACOG Op. at 3; *see also* Tr. at 39 (documenting Dr. Hamiel's testimony normal menstrual frequency for a woman in her twenties is 21-35 days); Pet'r's Ex. 20 at 5, ECF No. 64-3. The undersigned interprets this criterion to apply to frequency over two or more cycles.

[25] At the hearing, Dr. Hamiel testified that no menstruation for 90 days is not "normal." Tr. at 79.

There cannot be a better vehicle for the undersigned to use to sort out "normal" from "symptom" than one designed for that purpose by members of the medical profession themselves. Thus, the undersigned finds that for petitioners who were eighteen years old or younger at the time the condition arose, if the condition qualifies for evaluation on the ACOG chart, it constitutes a symptom for purposes of the Vaccine Act. For petitioners who were over eighteen years old at the time the condition arose, the chart also applies, except that periods that should be evaluated include those that occur more frequently than every 21 days or less frequently than every 35 days. *See* ACOG Op. at 3.[26]

Finally, as to contraceptives' impact on this analysis, Hillard specifically limited her discussion "only to bleeding on young women who are *not* taking any hormonal therapy such as birth control." Hillard at 6. All of the experts at the hearing agreed that hormonal therapy would mask POI symptoms. Tr. at 115, 161, 387-88. The ACOG Opinion recommends blood collection for screening before hormonal treatment is begun, ACOG Op. at 4, as did Doctors Hamiel, Tr. at 95-97, and Frankfurter, Tr. at 377, at the hearing; although, both experts acknowledged that such testing is often not performed before hormonal treatment is started. Tr. at 95-97, 112-13, 387-92.

Based on that information, the undersigned makes the following findings regarding how contraceptive use will inform the undersigned's findings concerning the first symptom of POI for purposes of the statute of limitations:[27]

1. If the form of contraceptive used was non-hormonal, i.e., a copper IUD without hormones,[28] condom/diaphragm, spermicide, the ACOG criteria apply as discussed above, without changes;

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[26] To the extent Petitioner argues that this interpretation of the Vaccine Act's statute of limitations violates the Fifth Amendment on Equal Protection and Due Process Grounds, *see* Pet'r's Post Hr'g Br. at 11-13, the undersigned concurs with the reasoning articulated in numerous decisions to the contrary, all of which hold that the Act's statute of limitations does not violate the Constitution merely because it bars certain petitioners from bringing a claim before they knew, or even could have known, that their injuries were vaccine-related. *See, e.g.*, *Cloer v. Sec'y of HHS*, 85 Fed. Cl. 141, 150-51 (2008), *rev'd on other grounds*, 603 F.3d 1341, *aff'd en banc*, 654 F.3d 1322 (Fed. Cir. 2011); *Leuz v. Sec'y of HHS*, 63 Fed. Cl. 602, 607-12 (2005); *Wax v. Sec'y of HHS*, No. 03-2830V, 2012 WL 3867161, at *6-8 (Fed. Cl. Spec. Mstr. Aug. 7, 2012); *Blackmon v. Am. Home Prods. Corp.*, 328 F. Supp. 2d 647, 655-57 (S.D. Tex. 2004); *Reilly ex rel. Reilly v. Wyeth*, 876 N.E.2d 740, 753-54 (Ill. App. Ct. 2007).

[27] This decision expresses no opinion concerning the effect, if any, of contraceptive use on the question of causation in a POI case.

[28] Dr. Frankfurther indicated that non-hormonal copper IUDs may affect the volume of flow but do not influence the cycle length or frequency. Tr. at 422.

2. By definition, a contraceptive is "an agent that diminishes the likelihood of or prevents conception." Contraceptive, *Dorland's*. Therefore, if the medical records show that a hormonal contraceptive was prescribed for its primary purpose, that is, for contraception, rather than as treatment for menstrual irregularities; or if the medical records are silent as to the purpose of the prescription and the contraceptive use spanned the date on which the statute of limitations would have begun to run; the statute of limitations will not preclude the claim;
3. If the medical records indicate that the hormonal contraceptive was prescribed to treat menstrual irregularities, or if menstrual irregularities were a reason for the medical visit that resulted in the prescription of the contraceptive, then the undersigned will find that the menstrual irregularities were not "normal," but resulted in treatment, and therefore constituted a symptom for purposes of the statute of limitations.

C. Application of the Onset Symptom Criteria to the Present Case

Petitioner filed her petition on April 18, 2014, *see* Pet.; her petition is therefore time-barred if "the first symptom or manifestation of onset" of her alleged vaccine injury, POI, occurred before April 18, 2011, *see* 42 U.S.C. § 300aa-16(a)(2). Petitioner asserts that the statute began to run on August of 2012, when she ceased menstruating. Pet'r's Post Hr'g Br. at 2. Respondent asserts that the statute was triggered in March 2010, when Petitioner's menstrual cycle shortened from 28-29 to 25 days. Resp't's Post Hr'g Br. at 3. Alternatively, Respondent asserts that the limitations period dates from late 2010, based on Petitioner's report to her doctor, on May 10, 2011, of six months of less frequent, heavier, and longer menstrual periods, Pet'r's Ex. 2 at 17-18, corroborated by her report, on January 15, 2013, that her oligomenorrhea had begun two years earlier, Pet'r's Ex. 2 at 11-12. Resp't's Post Hr'g Br. at 3.

Petitioner was 26 years old on April 18, 2011. The latest date on which she could have filed her petition without it being barred by the statute of limitations. In 2005 and 2006, her menstrual cycle was regularly 28-29 days. Pet'r's Ex. 6 at 5-7. At that time, she was using a non-hormonal form of contraception, a Paragard (copper) IUD. *See* Pet'r's Ex. 2 at 8-10; Pet'r's Ex. 6 at 5-6.

The undersigned agrees with Petitioner that the apparent shortening of Petitioner's menstrual cycle to 25 days as of March 31, 2010, *see* Pet'r's Ex. 2 at 21, did not constitute the first symptom or manifestation of onset of POI, because the 25 day cycle was still within the "normal" parameters for a woman of 25 years—a 21-35 day cycle. However, as of late 2010, Petitioner's menstrual cycle vital sign was not normal pursuant to at least two and possibly as many as four of the ACOG Opinion's criteria:

1) Her periods were regular, occurring monthly, as of 2005 and 2006, *see* Pet'r's Ex. 6 at 5-7, and then became *markedly* irregular in November or December 2010, as illustrated by the fact that her last menstrual period as of May 10, 2011, was almost three months earlier, February 21, 2011, and by her report to her gynecologist at the May 10, 2011, visit that her periods had become less frequent, heavier, and longer. Pet'r's Ex. 2 at 17-18.
2) Beginning in November or December 2010, her periods occurred less frequently than every 35 days, as illustrated by the fact that her last menstrual period as of May 10, 2011, was almost three months earlier, February 21, 2011, and by her report to her gynecologist at the May 10, 2011, visit that her periods had become less frequent, heavier, and longer. *Id.*
3) (and (4)) She reported heavier and longer periods beginning in November or December 2010, which may have lasted more than seven days and may have required frequent pad or tampon changes. *Id.*

Thus, as of November or December 2010, Petitioner's menstrual pattern was no longer "normal," but had become symptomatic of potential "disease or derangements in normal health." *See* Hillard at 8; *see also* Tr. at 67-68 (documenting Dr. Hamiel's testimony that that she would probably do a work-up on a woman who had regular periods (21-35 days) and then became more irregular (more than every 35 days)). The undersigned finds that this development of menstrual irregularity constituted the first symptom of Petitioner's alleged vaccine-caused injury, POI.

IV. CONCLUSION

Based on the foregoing analysis, the undersigned finds that the first symptom of Petitioner's injury was November or December 2010. Because that date precedes the statute of limitations deadline by five to six months, the undersigned concludes that Petitioner's claim is time-barred. Her petition therefore must be, and is hereby, **DISMISSED**.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court is directed to enter judgment herewith.[29]

/s/ Lisa D. Hamilton-Fieldman
Lisa D. Hamilton-Fieldman
Special Master

[29] Pursuant to Vaccine Rule 11(a), the parties can expedite entry of judgment by filing a notice renouncing the right to seek review by a United States Court of Federal Claims judge.